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TITLE: Development of Novel Therapeutics for Neglected Tropical Disease Leishmaniasis

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**13. SUPPLEMENTARY NOTES**

**14. ABSTRACT**
We undertook planning of kick off coordination meeting. A low dose infection model of CL was validated. A large scale synthesis of PEN optimized and in vitro studies were performed revealed that PEN alters parasite lipidome. Further studies were undertaken using sythetic PEN (sPEN) which showed that sPEN is effective in vivo in treatment of L. donovani infection. We have also synthesized ten analogues of PEN were synthesized as well as established synthesis of DNER. Testing of these compounds under way

**15. SUBJECT TERMS**
Pentalinonsterol, Leishmania, cutaneous leishmaniasis, treatment

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## Introduction

The following section describes at accomplishments and Changes/problems concerning our project W81XWH-14-2-0168 titled "Development of Novel Therapeutics for Neglected Tropical Disease Leishmaniasis" from October 1, 2014 to October 30, 2015.

## Key words

Pentalinonsterol, *Leishmania,* cutaneous leishmaniasis, treatment

## Accomplishments

- Undertook planning of kick off coordination meeting
- Large scale synthesis of PEN optimized
- Established and tested *in vitro* assays for mechanistic lipidomic studies
- Ten analogues of PEN were synthesized and their in vitro testing is under way
- A publication has resulted from the research partly supported by this grant (*J Nat Prod. 2015 Apr 24;78(4):653-7*).
- Low dose infection model of CL is validated for in vivo studies
- Stable analogues of PEN have been synthesized
- Synthetic DNER is being tested *in vitro*

## Impact

- Our work on synthetic PEN was selected for presentation at The **2015 Military Health System Research symposium** was held from 17 Aug to 20 Aug 2015 at the Marriott Harbor Beach Resort, Ft. Lauderdale, FL
- Our work on efficacy of synthetic PEN in treatment of VL was published in ACS Infectious Diseases. (ACS Infect. Dis., ***2015***, 1 *(10), pp 497–506*)
- This work was also highlighted in ACS Newsletter Chem and Eng News (http://cen.acs.org/articles/93/web/2015/09/Plant-Used-Traditional-Mayan-Medicine.html)

- PEN was also highlighted as Molecule of the Week by ACS (http://www.acs.org/content/acs/en/molecule-of-the-week/archive/p/pentalinonsterol.html)

## Changes/Problems

- Hiring of personnel to work on this project was delayed due to unavailability of suitably qualified personnel in the initial application pool
- Start of project was also delayed due to relocation of our animals to a new BSL II animal facility due to some technical issues in our current animal facility.
- Some technical issues were faced for detecting Luc-*L. mexicana* parasites in mice by imaging. We developed an alternate strategy involving manual counting in case we are not successful in using Luc-*L. mexicana*
- We are some technical issues in establishing large scale synthesis of DNER but they were resolved
- We were having some technical issues with long term stability of sPEN. This could be due to batch-to-batch variation. We are checking this possibility

**Products:** None

**Participants and other organizations**

The Ohio State University
College of Medicine, College of Pharmacy and College of Arts and Sciences

**Special Reporting Requirements:** None